HAEMATOLOGICAL ABNORMALITIES IN CIRRHOSIS OF LIVER.

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CERTIFICATE

This is to certify that the dissertation titled "**THE HAEMATOLOGICAL ABNORMALITIES IN CIRRHOSIS OF LIVER** is the Bonafide original work of **Dr. M. SHANMUGANANTHAN** in partial fulfillment of the requirement for M.D. Branch –I (General Medicine) examination of the Tamil Nadu Dr. M. G. R. Medical University to be held in March 2007. The period of study is from August 2005 to September 2006.

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DECLARATION

I **Dr. M. SHANMUGANANTHAN**, solemnly declare that the dissertation titled, "**HAEMATOLOGICAL ABNORMALITIES** was done by me at Govt. Stanley Medical College and Hospital during 2005– 2006 under the guidance and supervision of my unit chief **Prof. Dr. K. RAJENDRAN, M.D.,**

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HAEMATOLOGICAL ABNORMALITIES IN CIRRHOSIS OF LIVER

INTRODUCTION

Cirrhosis is one of the commonest diseases affecting man. Hepatic cirrhosis can occur at any age and often causes prolonged morbidity. It frequently manifests itself in younger adults and is an important cause of premature death.

Liver disease produces a diverse range of haemotological effects. Liver disease can affect all the formed elements of blood RBCS, WBCS, and platelets. Liver disease has important effects on haemostasis.

The liver plays a central role in the synthesis of many proteins and the maintenance of metabolic homeostasis. It is therefore not surprising that the development of clinically important liver diseases is accompanied by diverse manifestations. Although some functions are more sensitive than others, the liver has considerable reserve capacity, so, minimal or even moderate cell injury may not be reflected by measurable functional changes.

Impaired liver functions are most evident in the patient with advanced liver disease, and the manifestations are similar regardless of initial insult. To a varying degree, similar abnormalities are observed in patients with severe chronic hepatitis, micronodular cirrhosis and post necrotic cirrhosis.

CIRRHOSIS OF THE LIVER.

Cirrhosis is obtained from the Greek word" KIRRHOS" meaning tawny or yellowish brown. It was coined by **Laennec.**

Cirrhosis is pathologically defined entity that is associate with a spectrum of clinical manifestations. The cardinal pathological features are,

I. Fibrosis is present in the form of delicate bands (portal-central, portal- portal, central – central) or broad scars replacing multiple adjacent lobule.
II. The parenchymal architecture of the entire liver is disrupted by inter connecting fibrous scars.
III. Parenchymal nodules are created by generation of hepatocytes.

Several features should be underscored.

1. The changes in cirrhosis affect the whole liver but not necessarily every lobule, Focal injury with scarring does not constitute cirrhosis. The parenchymal injury and consequent fibrosis are diffuse extending throughout the liver. Focal injury with scarring does not constitute cirrhosis.

2. Nodularity is requisite for the diagnosis and reflects the balance between regenerative activity and constrictive scarring.

3. The fibrosis once developed is generally irreversible.

4. Destruction of the liver architecture causes distortion and loss of the normal hepatic vasculature with the development of portal systemic vascular shunts.

CLASSIFICATION BASED ON ETIOLOGY.

1. Alcoholism.
2. Post infective- chronic viral infection: HIV, HBV+HDV, HCV.
3. Drugs and toxins.
4. Auto immune chronic liver diseases.
5. **Metabolic disorders**.
    a) Haemochromatosis.
    b) Wilson's disease.
    c) Alpha1 anti-trypsin deficiency.
    d) Cystic fibrosis.
    e) Glycogen storage diseases.
    f) Galactosemia.
    g) Hereditary Fructose Intolerance.
    h) Hereditary Tyrosinemia.
    i) Ornithine transcarbamylase deficiency.
    j) Abeta lipoproteinaemia.
    k) Porphyria.
6. Biliary tract disease(prolonged)
    a) Extra hepatic biliary obstruction.
    b) Intra hepatic biliary obstruction.
    c) Primary biliary cirrhosis.
    d) Primary sclerosing cholangitis.
7. Venous outflow obstruction.
    a) Veno occlusive disease.
    b) Budd chiari syndrome.
    c) Cardiac failure.

8. **Others**.

a) Obesity.

b) Diabetes Mellitus.

c) Intestinal bypass.

d) Sarcoidosis

e) Syphilis.

f) Indian Childhood cirrhosis.

CLINICAL FEATURES OF CIRRHOSIS.

Cirrhotic patients commonly present with the following symptoms. They are,

1. Anorexia and nausea.
2. Haemetemesis / malena.
3. Fatigue and weight loss.
4. Abdominal distension / pedal edema.
5. Jaundice.
6. Low grade fever
7. loss of libido

Clinical manifestations in cirrhosis are due to

1. Portal Hypertension
2. Prolonged alcohol intake
3. Diminished Hepato cellular function.

The following stigmata of chronic liver disease should be looked for.

FACE:

1. Parotid enlargement.
2. Madarosis.
3. Telangiectasia
4. Xanthelasma
5. Cushingoid Facies.
6. Pallor.

HANDS:

1. Anaemia
2. Whitenails.
3. Dupuytren's contracture.
4. Palmar erythema
5. Clubbing.

NUTRITION:

1. Muscle wasting
2. Glossitis
3. Angular stomatitis.
4. Anaemia

SKIN:

1. Spider Naevi
2. Scanty body hair.
3. Slate gray pigmentation.
4. Scratch marks.

ENDOCRINE ABNORMALITIES:

1. Gynaecomastia.
2. Testicular atrophy.

FEATURES DUE TO PORTAL HYPERTENSION:

1. Splenomegaly.
2. Ascites.
3. Oesophageal varices.
4. Anorectal varices.
5. Dilated veins over the abdomen (Caput Medusae)

COMPENSATED vs. DECOMPENSATED CIRRHOSIS.

COMPENSATED CIRRHOSIS.

The disease may be discovered at a routine examination or biochemical screen or at operation undertaken for some other condition. Cirrhosis may be suspected if the patient has mild pyrexia, vascular spiders, palmar erythema or unexplained epistaxis or edema of ankles. Firm enlargement of the liver and splenomegaly are helpful diagnostic signs. Vague morning indigestion and flatulent dyspepsia may be early features in the alcoholic cirrhotic. Confirmation should be sought by biochemical tests and if necessary by liver biopsy. Biochemical test may be quite normal in this group. The most frequent changes are a slight increase in the serum GGT level.

DECOMPENSATED CIRRHOSIS.

The patient usually seeks medical advice because of ascites or jaundice. General health fails with weakness, muscle wasting and weigh loss. Continuous mild fever is often due to gram negative bacteremia, to continuing hepatic cell necrosis or to complicating liver cell CA. Foetor hepaticus may be present. It is the commonest cause of hepatic encephalopathy. Jaundice implies that liver cell destruction exceeds the capacity for regeneration and is always serious. The deeper the jaundice, the greater the inadequacy of liver cell function. The liver may be enlarge with firm regular edge or contracted and impalpable. The spleen may be palpable.

ROLE OF LIVER IN HAEMOPOIESIS.

The liver has an important role as a haemopoietic organ in foetal life. It is the primary site of erythropoiesis in the foetus from the ninth to twenty fourth week of gestation. Thereafter bone marrow becomes the major source of RBC. Extra medullary haemopoiesis is found in the adult liver in certain pathological states. Eg.

Myelofibrosis. Granulocytes precursors and megakaryocytes are also present I foetal liver but production does not become significant until haematopoiesis becomes established in the marrow.

In adult the kidney is the main source of erythropoietin and liver is the site of clearance, however the liver can produce this hormone in the presence of uraemia, in response to hypoxia or hemolysis or when hepatocytes are regenerating.

The liver also plays an important role in the metabolism of iron, vitamin B12 and folate. Thus although the liver disease in adults rarely causes haemotological complications solely on the basis of defective haemopoiesis. The liver may, none the less have an importance role in facilitating bone marrow function. The precise mechanisms are not understood but disturbances of them may explain the suboptimal marrow response to Anaemia and thrombocytopenia seen in patients with liver disease.

SYNTHESIS OF COAGULATION PROTEINS

The liver is the main site of production of all the coagulation proteins except von willibrand Factor. The important synthetic role of liver is supported experimentally by showing a fall in factors I, II, VII, IX, X, XI, XII following chemically induced hepatic necrosis.

Factor VIII is the synthesized by the hepatocyte and also in many other tissues and also is largely spared in liver diseases. Vitamin K dependant coagulation proteins are synthesized in the liver in a precursor form. They are II, VII, XI, and X.

NORMAL COAGULATION AND THE ROLE OF THE LIVER.

Under normal conditions, blood circulates through the vasculature without appreciable coagulation or heamorrhage. When vessel injury occurs, three haemostatic responses are initiated.

1. The vessel constricts
2. Platelets adhere at the site of damage and subsequently aggregate and
3. Fibrin clot is formed and modified

The haemostatic response occurs in a stepwise, integrated manner. In primary haemostasis, vessels constrict and a temporary platelet plug is formed. Secondarily the platelet plug is reinforced with a durable fibrin clot. The fibrin clot is modified an after tissue healing ultimately dissolve by fibrinolytic components. The failure of any part of the haemostatic response may contribute to haemorrhage. The coexistence of multiple defects in the haemostatic system may have an additive effect, resulting in a profound haemorrhagic catastrophe.

Vasoconstriction is an immediate but probable minor response to vascular injury. Small arteries and veins contract so as to decrease blood flow to the area. If haemorrhage occurs in a closed compartment such as joint space local pressure causes collapse of small vessels, thereby contributing to local control. In the absence of local tissue tension, as in gastro intestinal bleeding or haemorrhage from a large vessel, bleeding is more difficult to control.

Platelets serve two functions. First they form a primary haemostatic plug. Second, they serve as a template for the generation of fibrin by way of the coagulation cascade. Platelet plug formation occurs in two phases. Platelet adhesion, which occurs within seconds, followed by platelet aggregation, which is complete within minutes. Platelet adhesion to the injured vessel requires the secretion of von willibrand Factor by

endothelial cells and the availability of platelet membrane glycoprotein Ib as a receptor for von willibrand Factor. Once adhesion occurs, platelets undergo a shape change with a coincident release of various mediators, including ADP, which stimulates platelets to aggregate and form the primary platelet plug. The aggregated platelets then provide the surface on which the fibrin plug is formed. In addition platelets serve as a source of phospholipids, in the form of platelet factor 3 required for the conversion of prothrombin to thrombin by factor X a.

The exposed subendothelial components activate the coagulation cascade, either through contact activation of the intrinsic pathway or through expression of tissue factor at the site of injury with consequent extrinsic pathway activation. It is now recognized that the intrinsic and extrinsic pathway are not entirely independent of each other. Invitro and invivo studies support the observation that factor VII – tissue factor also activates factor IX. Through a complex sequence of reactions, clotting factor precursors are converted to their active form with the eventual generation of thrombin. Thrombin then transforms fibrinogen to fibrin is cross linked by factor XIIIa to form a stable fibrin clot.

When fibrin is formed, plasminogen is bound to the clot. Tissue plasminogen activator is released from endothelial cells and then binds to the fibrin clot. On the fibrin surface, plasminogen is cleared, plasmin is generated and fibrin degradation ensues. Remodeling and eventual dissolution of the clot permit subsequent wound healing with the formation of fibrous tissue. In abnormal states, such as disseminated intravascular coagulation, plasmin may also be present in blood, and degrade fibrinogen and factors V, VIII, XIII.

Modulation of coagulation and fibrinolysis occurs at various sites as listed in table (1). Control of coagulation is achieved by several measures. The liver inactivates activated factors further; natural inhibitors to various factors are present in plasma.

Antithrombin III (ATIII) is a major inhibitor of thrombin as well as factor XIIa, XIa, Xa and IXa. AT III also inhibits plasma kallikrein and plasmin. The activity of AT III is increased thousand fold in the presence of heparin, heparin or contact with endothelial cells, which are coated with heparin sulphate.

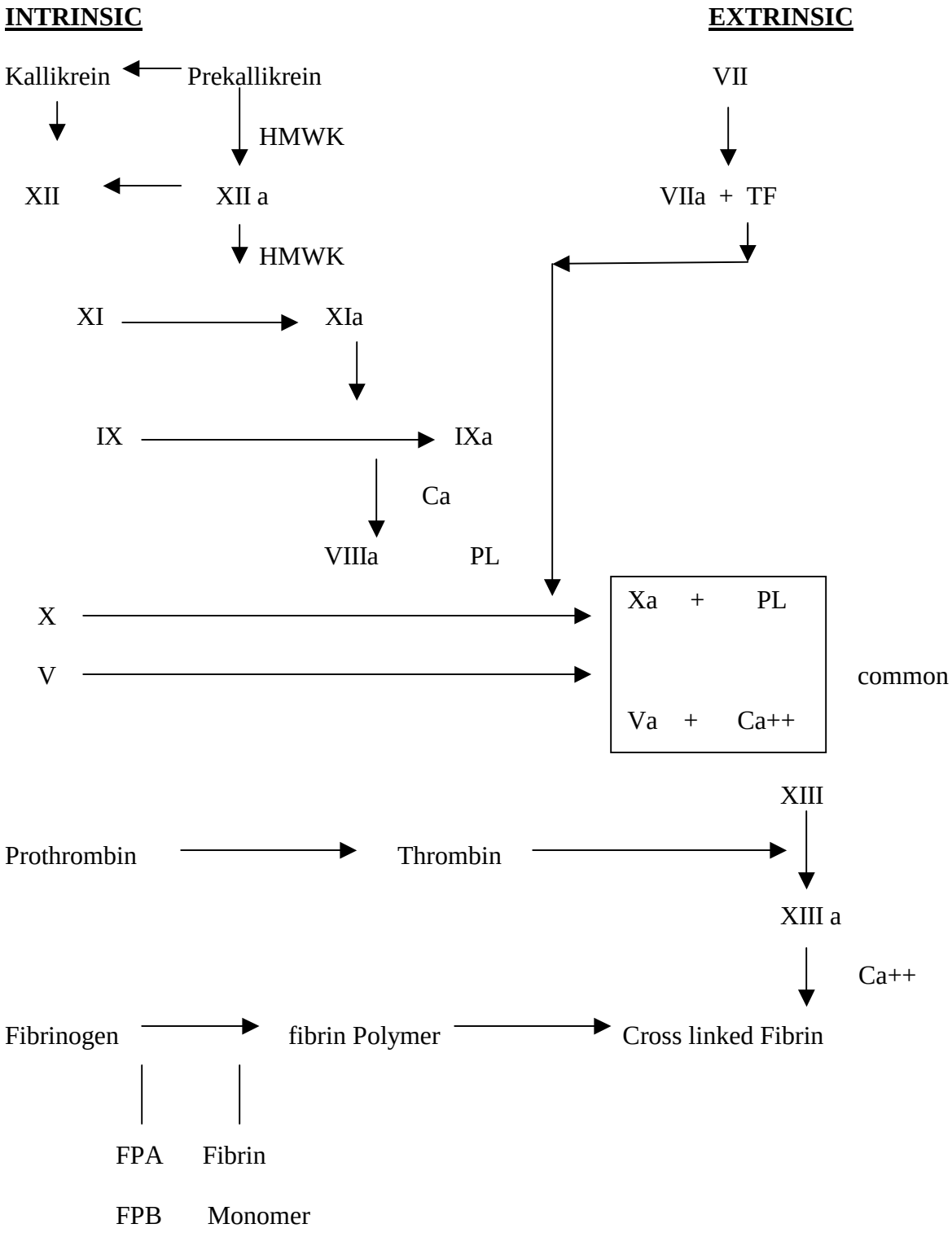
Protein C is a second major inhibitor. This vitamin K dependant glycoprotein is synthesized in the liver and inactivates factors Va, VIIIa. In addition, protein C enhances fibrinolysis by inactivating plasminogen activator inhibitor type 1. Protein C is activated when thrombin is bound to the endothelial cell membrane protein thrombomodulin.

Both anticoagulant and profibrinolytic activities of protein C are accelerated in the presence of the cofactor protein S, another vitamin K dependant protein. Activated protein C is inactivated by Alpha 1 antitrypsin and protein C inhibitor.

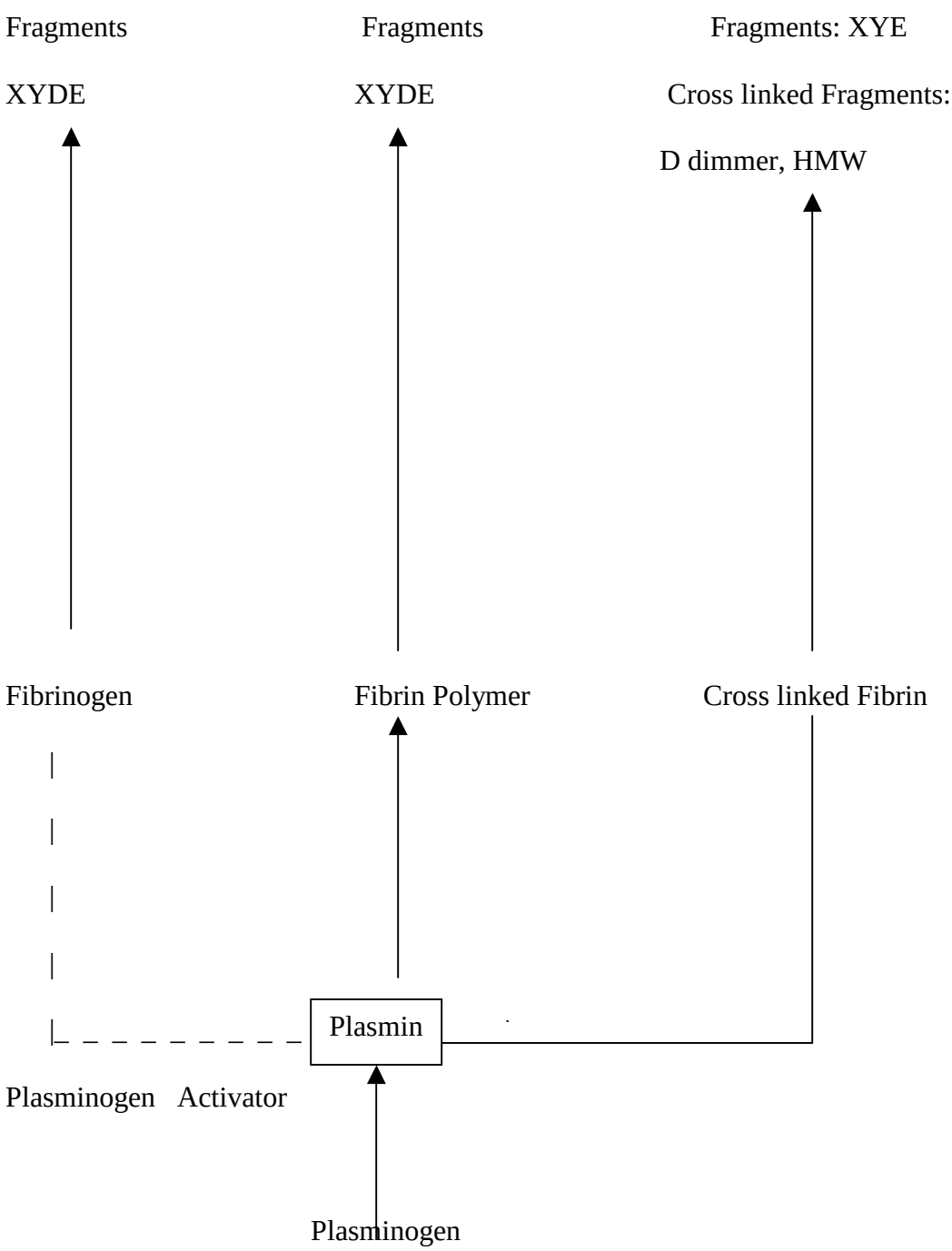
Heparin cofactor H, a glycoprotein synthesized by liver, inactivates thrombin in the presence of heparin or dermatan sulphate. Extrinsic pathway inhibitor (also called lipoprotein associate coagulation inhibitor) inhibits coagulation, initiated by VIIa tissue factor complex by binding to factor Xa. The site of synthesis of extrinsic pathway inhibitor is still not certain. The major inhibitor of plasmin is alpha2 antiplasmin which is synthesized in liver. Alpha2 macroglobulin, a second line inhibitor of plasmin and thrombin is synthesized by macrophages and possibly hepatocytes. TPA is inhibited by plasminogen activator inhibitor I, which is secreted by endothelial cells but also found in platelets.

The liver plays a central role in haemostasis. In addition to its synthetic function the liver serves as a key site for clearance of activated clotting factors and plasminogen activators.

OVERVIEW OF COAGULATION CASCADE



FIBRINOLYTIC PATHWAY



AIM OF THE STUDY

1. To detect various Haematological Abnormalities in Cirrhosis.

2. To Detect Reversible Factors like Anaemia, thrombocytopenia. So that correction of them may make the patients life less miserable.

3. To assess haemostatic functions of the liver in cirrhosis.

REVIEW OF LITERATURE.

This discussion will highlight the intriguing newer concepts more in detail than the established ones.

ALTERATION IN THE HAEMATOLOGICAL FUNCTIONS IN CIRRHOSIS.

Liver disease may result in abnormalities of haemopoiesis ranging from morphological changes to varying degree of anaemia. White cell abnormalities also occur varying from Leucopenia to leucocytosis. Disturbed haemostasis is common and results from thrombocytopenia and impaired synthesis of coagulation factors.

ANAEMIA IN LIVER DISEASES.

Anaemia occurs in upto seventy five percent of patients with chronic liver disease. It is characteristically of moderate severity and is either normochromic normocytic or moderately macrocytic. The anaemia of liver disease results from

1. Heamodilution
2. Shortened RBC survival.
3. Reduction of the capacity of marrow to respond to anaemia.
4. Splenomegaly and hypersplenism resulting in pooling of RBCs & excessive destruction of RBCs.
5. Haemorrhage.
6. Haemolysis.

The anaemia in liver disease usually varies from 7gm/dl to 13gm/dl. Severe anaemia below 6gm/dl is very rare.

IRON METABOLISM IN CIRRHOSIS.

A low or normal iron conc. with low or normal total iron binding capacity is frequently found in uncomplicated cirrhosis and is compatible with the anaemia of chronic disorder which is commonly seen in inflammatory and neoplastic disorders. Iron deficiency is frequently found as a result of previous GI haemorrhage and the resulting anaemia often responds to oral iron therapy.

An important practical point is that hepatic inflammation and necrosis tends to increase serum ferritin. So that a raised value does not necessarily indicate iron over load, and a normal value does not exclude iron deficiency. The rise in RBC Mean Corpuscular volume which accompanies liver disease and alcoholic ingestion can also mask iron deficiency which is normally characterized by the lowering of Mean Corpuscular Volume.

Iron in plasma is bound to a beta globulin transferring and total iron binding capacity largely depends on transferring conc. measurement of total iron binding capacity gives rough estimation regarding the iron deficiency.

VITAMIN B12 AND FOLIC ACID METABOLISM.

The liver is important storage organ for both vitamin B12 and folic acid. Liver disease leads to several clinically significant disorders of their metabolism. Lack of either vitamins leads to megaloblastic haemotopoiesis. Alcohol can inhibit Vitamin B12 absorption. Chronic alcoholism and dietary deficiency are the major cause of folate abnormalities reported in alcoholic cirrhosis are either due to direct toxicity of alcohol or to the associated nutritional deficiency. Excessive intake of alcohol will have a direct toxic effect on blood and bone marrow and will result in metabolic

abnormalities and consequent haematopoietic abnormalities, RBCs, WBCs and platelet production may all be affected.

Most of the cirrhotic patients are undernourished for years together, under-nutrition itself will contribute to further cirrhosis. The dietary intake is below par even with proper medical advice and treatment. Loss of appetite, fullness of the abdomen, pain abdomen may limit the intake of food in these patients. Indigestion and vomiting may also contribute to some extent. Ultimately daily intake of protein and carbohydrates are much reduced than what is needed.

Protein in adequate amount is required for the erythropoiesis. Deficiency of this protein causes impaired erythropoiesis, leading on to anaemia. Deficiency of other vitamins like pyridoxine, Vit-C is likely to cause anaemia in these patients. More than 75 % of 65 cases with chronic alcoholic liver disease studied, showed abnormality of RBC production. When markedly anaemic patients were studied high incidence of both megaloblastic and ringsideroblastic changes were seen. (Eichiner R and Hillmans)

According to Cirera I, Panes J, Bordas J.M., LLach J, Busch J., Pique J.M., Teres J. in their study showed that anaemia increases gastric blood flow in cirrhotic and non cirrhotic patients. (Source: GI endoscopy 1995- Nov.). In anaemic patients the index of the Hb Conc. of the gastric mucosa assessed by reflectance spectrophotometry was significantly decreased in Cirrhotic and non cirrhotic, where as the index of the O2 saturation was increased. In conclusion, chronic anaemia is associated with an enhanced gastric blood flow and gastric mucosal O2 index, despite a decrease in Gastric Hb Conc. Cirrhotic anaemia further promotes further increment in its basal gastric hyperemia.

Authors- Siciliano M. Tomasello D. Miloni A. Ricerca B.M. Sterti S. Rossi L. found out reduced serum levels of immunoreactive erythropoietin (EPO) in patients with cirrhosis in chronic anaemia, (Source: Hepatology – 1995, Oct. 1132~5). Chronic anaemia is frequently seen inpatients with cirrhosis. To investigate the possible role of EPO in the pathogenesis of anaemia in cirrhosis, they measured the immunoreactive EPO levels and the respective Hb Conc. In 48 anaemic & non anaemic cirrhotic patients and in a control group of healthy subjects and in patients with iron deficiency anaemia. A blunt EPO response to anaemia in cirrhosis. The study also showed that EPO levels for a given degree of anaemia were further reduced in patients with a more severe disease suggesting the close relationship between cirrhosis and the mechanism involved in the derangement of EPO feedback system.

HEMOLYTIC SYNDROMES IN LIVER DISORDERS.

Many of the features of hemolytic anaemia like raised bilirubin ConC., Reduced or absent haptoglobin and shortened RBC survival are found in uncomplicated liver disease. One study demonstrated RBC life span to be reduced to about 50 % in patients with cirrhosis.

The Cause of hemolytic anaemia may be grouped broadly into extra corpuscular and intra corpuscular. There are two major extra corpuscular causes. They are Hypersplenism and lipid abnormalities. The latter induces alterations in the RBC membranes. The spleen plays a central role in conditioning the RBC, a process where by the spleen progressively erodes the membranes of RBC entrapped within its specialized circulation to cause spherocytes and hemolysis.

The finding in hyperlipemic variety of hemolytic anaemia in cirrhosis differs sharply. Episodes of hemolysis appear to be precipitated when alcoholics indulge in heavy drinks; characteristically blood shows hypercholesterolemia with or without increased values of lipid. Hemolysis in this group probably relate to the presence of abnormal

serum lipids or abnormal distribution of serum lipids. Abnormality in serum lipids seems to alter the RBC membranes to make it more fragile. Subsequently, this fragility leads to hemolysis of RBC and leads to hemolytic anaemia.

	Zieves syndrome or Hyperlipemic anaemia	**Hypersplenism with anaemia**
Clinically	Mild	Moderate to severe
Fatty infiltrations	Frequent	Infrequent
Hemoptysis	Marked	Variable
Splenomegaly	Absent	Marked
Lipids	Increased	Normal
Fragility	Increased	Normal
Bilirubin ratio	Not decreased	Decreased
Bone marrow hyperplasia	Variable	Variable
Duration of illness	Brief	Prolonged
Improvements	Marked	Slight or absent

ABNORMALITIES IN RED BLOOD CELL SHAPE.

ABNORMALITY	LIVER DISEASE
Macrocytes	Alcoholic cirrhosis
Target cells	Cirrhosis
Spherocytes	Zieve's syndrome associated with alcoholic cirrhosis
Echinocytes, Acanthocytes	Severe form of cirrhosis
Stomatocytes, tear drop, poikilocytes	Alcoholic cirrhosis

Above mentioned table indicate various abnormal RBC shape. Macrocytosis is found in approximately two third of patients with chronic liver disease and upto ninety % of alcoholics.

BINGAM in his classic papers described three types of Macrocytosis in liver disease. Thin Macrocytosis, target Macrocytosis and thick Macrocytosis. Thin macrocytosis is common, characterized by increased RBC diameter with slight increase in MCV. Target macrocytosis is one where thin macrocytes have formed target cells. Thick or true macrocytosis is associated with a marked increase in MCV which is less common in cirrhosis.

The precise mechanism responsible for the macrocytosis of the liver disease is unclear but increase in RBC membrane cholesterol and phospholipids contents is likely to be important. Additional mechanisms for the macrocytosis would include the reticulocytosis associated with hemolysis or bleeding, and disturbances of Vit.B12 and folic acid metabolism.

BINGAM concluded from cross transfusion studies that there was an intrinsic abnormality in bone marrow erythropoiesis, and it is likely that alcoholics and patients with chronic liver disease do indeed have disturbed erythropoiesis which is macronormoblastic.

In Routine blood films, Target cells are seen in most patients with significant liver disease as their RBC membrane contains more cholesterol or more cholesterol and phospholipids, than that of normal cells. The surface area expands without corresponding changes in volume and as a consequence the cell become “BOWEL or SAUCER” shaped. Although this shape is obvious in wet films and on scanning electron microscopy, drying prior to staining distorts the cell and in conventional blood films they appear “target cells”. As darker cells are also seen in familial LCAT deficiency, their presence in liver disease may result from low LCAT activity and transfer of lipid to RED cell s from cholesterol rich Lipoprotein particles. As volume should not be increased by expansion of the membranes, target cell formation is unlikely to be the reason for the macrocytosis often seen in liver disease.

In conventional blood films RBC from patients with cirrhosis often appear normal in shape except for the presence of target cells. However in wet films or on scanning electron microscopy, many patients have speculated RBC or echinocytes in the blood. Sometimes when the numbers are very large and cells have many spicules, spiky RBCs are seen in conventional blood films.

The presence of echinocytes appears to be related to changes in HDL, Purified HDL from blood containing echinocytes transforms normal RBCs. The cells rapidly revert to normal incubation with albumin or normal HDL. The HDL induced echinocytosis is not accompanied by enrichment for echinocytogenesis in liver diseases; although, one would expect the cells in liver disease do have a high cholesterol phospholipids

ratio of abnormal HDL by the RBC surface. The pathophysiological significance of shape changes in RBCs is unknown, and there appears to be no clear relationship between the echinocytes and the Hb level.

RBC of bizarre shape are seen occasionally in Blood of cirrhotic in association with the hemolytic anaemia (SPUR CELL ANAEMIA). The term spur cell anaemia should only be applied when acanthocytes are present. Their shape is quite different from that of echinocytes but the distinction is not always consistently made. The cirrhosis is usually but not invariably, alcoholic in origin. The liver disease tends to be quite severe with jaundice, ascites, encephalopathy and, or GI Haemorrhage preceding or following the development of hemolysis; although the patients may survive many months with acanthocytosis, the prognosis of the underlying liver disease is poor. Only a small proportion of the RBC in these patients is acanthocytes. Most of the remaining cells are typical echinocytes. The echinocytes, but not the acanthocytes have been produced invitro incubating normal RBCs in sera of patients with spur cell anaemia, it was suggested that the shape change is caused by marked elevation of the membrane cholesterol Phospholipids ratio.

WBC CHANGES IN LIVER DISEASES.

WBC abnormalities in liver disease may be due to underlying disease or its therapy and range from neutrophilia to neutropenia and lymphopenia. Leucocytosis occurs in response to infections, Hemorrhage, hemolysis and malignancy. A mild leucopenia is frequently encountered in patients with chronic liver disease and reflects either hypersplenism or a toxic effect on bone marrow. In addition to causing leucopenia, alcohol has well recognized toxic effects on neutrophills and also on lymphocytic functions which cause defect in both cellular and humoral immunity.

Increased susceptibility to infection is well recognized in chronic liver disease and this is likely to be due to combination of mechanisms. Specific areas of Haemotological interests are disturbances of neutrophill function, lymphocytes function and complement activation. Neutrophill Chemotaxis has been found to be depressed in the presence of patients serum, although the chemotactic response of the cells themselves is normal in the presence of normal serum. This effect is due to low level of alternate pathway complement systems and reductions in these components have been reported in chronic liver disease. The high levels of IgA which are frequently found in patients with alcoholic cirrhosis and cryptogenic cirrhosis may form aggregates or complexes and thus inhibit chemotaxis.

LIVER DISEASE AND PLATELETS.

Defects of platelet functions and number are well documented in patients with chronic liver diseases and contributed significantly to their hemostatic abnormalities. A number of studies examined platelet kinetics in patients with chronic liver disease.
The studies have demonstrated a diverse etiology for thrombocytopenia of liver disease. They are

1. Shortened platelets mean life time.
2. Pooling of platelet within enlarged spleen.
3. Inability of the bone marrow to compensate adequately for thrombocytopenia.

There is no clear relationship between abnormalities of platelets kinetics and the severity of liver disease and very low counts are often seen with portal hypertension and spleenomegaly, in patients who have relatively normal LFT.

It has recently been suggested that impaired synthesis of thrombopoietic factor normally produced by the liver may contribute to the thrombocytopenia of liver disease. There is evidence that platelets responsiveness is impaired in chronic liver disease and their aggregation may be impaired by both intrinsic platelet defect and by circulating inhibitors of aggregation. The causes of the functional abnormalities are probably similarly to the underlying causes of the thrombocytopenia and included platelet activation, perhaps by adhesion to incompletely endothelialized sinusoids, enzymatic alterations of the platelet membrane and metabolic factor associated with the cirrhotic process or its causes.

Normal platelets enriched with cholesterol show increased aggregability by ADP and adrenaline. Platelets in liver disease tend to be cholesterol rich but their aggregability is diminished probably because the arachidonic acid content of the platelet phospholipids is reduced, this may diminished production of proaggregating TxA2.

A raised level of platelets associated Ig is found in a proportion of patients with chronic liver disease suggesting that antibody mediated platelet destruction may contribute it the shortened platelet survival in some patients.

THE EFFECT OF CIRRHOSIS ON HAEMOSTASIS.

Liver produces various proteins which help in the maintenance of normal haemostasis. It produces procoagulants, anti coagulants, profibrinolytics and anti fibrinolytics.

Vitamin K dependant coagulation proteins are synthesized in the liver in a precursor form. These non functional proteins are called “Protein induced in Vit. K absence” (PIVKA). The conversion of PIVKA factor to the biologically active form involves carboxylation of the alpha carbon of specific glutamic acid residue in the N-terminal regions.

Antithrombin III is a glycoprotein which is synthesized by both hepatocyte and endothelial cells. It behaves as an anti coagulants as evidenced by the observation that a relatively small reduction of serum antithrombin III is associated with an increased risk of venous thrombosis. The low level of serum antithrombin II in liver cirrhosis are due to impaired synthesis rather than increased metabolism.

An increased amount of fibrinogen is produce in cirrhosis. The fibrinogen that is produced in liver disease is often abnormal and shows defective polymerization. An excess amount of low molecular weight fibrinogen is produced. Acquired dysfibrinogenaemia occurs in any patients with chronic liver disease and seems to reflect the severity of the impairment of the liver function.

Accelerated fibrinolysis is a recognized complication of cirrhosis. In addition to synthesizing plasminogen, the liver also synthesizes the main plasmin inhibitor, alpha 2 plasmin inhibitor. There is also impaired clearance of plasminogen activators. Thus the mechanism of increased fibrinolysis is multifactorial and due to increased levels of circulating plasminogen activators, caused by decreased clearance and reduced inhibition of plasmin as a result of diminished synthesis of plasmin inhibitors.

The effects of chronic liver disease on Hemostasis are illustrated in the table below.

THE EFFECT OF LIVER DISEASE ON HAEMOSTASIS.

I. Decreased synthesis of proteins.

Coagulation	:	Factor XII, XI, IX, VII, II, Fibrinogen, prekallikrein, Kininogen.
Anticoagulant	:	Protein C and S, Antithrombin III.
Profibrinolytic	:	Plasminogen.
Antifibrinolytic	:	2-Antiplasmin, C-1 inhibitor, 2-Macroglobulin, histidine rich glycoprotein.

II. Synthesis of abnormal proteins.

Vitamin K dependant factors.

Factor VIII & Von willibrand Factor.

Fibrinogen.

III. Decreased clearance functions.

Activated Coagulation factors.

Plasminogen activators.

Thrombin Anti thrombin III complexes.

IV. Abnormalities of platelets.

DIC

DESIGN OF THE STUDY (MATERIALS AND METHODS)

This study was conducted in Government Stanley hospital, Chennai – 3, Between Sept-2005 to Aug-2006. Fifty patients suffering from cirrhosis were selected in random for the study. 42 of them were males & 8 were females.

Blood samples obtained from the patients were personally handed over to clinical pathological dept. The age group of the patients was from 20 to 65 years.

Age in years	**No. of patients**	**Percentage**
20 ~ 35	8	16
36 ~ 50	32	64
51~65	10	20

The majority of the patients were daily wage coolies, coming from lower socio-economic group. Their diet is particularly poor in protein. Past history of Jaundice was obtained in 16 patients. History f alcoholism was obtained in 36 patients. In the majority of patients Oesophageal varices seen in upper GI endoscopy were taken as indirect evidence while tissue proof obtained by performing the liver biopsy was considered to be direct evidence of cirrhosis.

USG abdomen was routinely performed in all the patients. In these patients in whom liver biopsy was not performed due to contraindication or in whom the procedure was not successful, the coarse heterogenous echotexture of liver found in these patients was considered to be the direct evidence for the cirrhosis. Bone marrow study was carried out in forty patients.

The following Haematological studies were carried out to assess red blood cell abnormality.

1. RBC count.
2. Heamoglobin Estimation.
3. PCV
4. MCV
5. MCHC
6. Peripheral Smear
7. Reticulocyte count

To assess white blood cell abnormality

1. Total WBC count
2. DC

To assess Haemostasis

1. Platelet count

2. Bleeding time / Clotting time
3. Prothrombin time

The proforma used for clinical, biochemical and Haematological evaluation is given below.

PROFORMA

Study in various haematological abnormalities in cirrhosis of liver

Name:

Age:

Sex:

IP No:

Presenting complaints:

History of Present illness

Nausea / Anorexia	Difficulty in breathing
Vomiting	Loss of weight
Haematemesis	Haematochezia
Malena	Constipation
Abdominal Distention	Diarrhoea
Swelling of legs	Jaundice
Oliguria	Mental Confusion
Abdominal Pain	Other Symptoms
Loss of consciousness	
Chest pain	

History of Past illness

Jaundice	Surgery
Tuberculosis	Needle pricks
Blood transfusion	Malignancy
Diabetes Mellitus	GI Bleed

Personal History

Alcohol

Smoking

Others

Family History

Chronic Liver Disease

Diabetes Mellitus

Others

Clinical Examination

General Examination

Built	Nourishment
Consciousness	Clubbing
Anaemia	Cyanosis
Jaundice	Lymphadenopathy
Pedal Edema	

Stigmata of chronic liver disease

Face	**Hands**
Telangiectasia	White nails
Xanthelasma	Dupuytren’s contracture
Paper monkey skin	palmar erythema
KF Ring	
Cushingoid Facies	
Parotid Enlargement	

Skin	**Endocrine**
Spider naevi	Gynaecomastia
Scanty body hair	Atrophic testes
Slate grey pigmentation	
Scratch Marks	

Vital Signs

Pulse

BP

Respiratory Rate

Temperature

Systemic Examination

CVS :

RS :

CNS :

ABDOMEN: Ascites

Splenomegaly

Dilated Veins over abdomen

Hernia

Hydrocele

Investigation

Blood

TC
DC
RBC
HB%
PCV
Urea
Sugar

MCV
MCHC
Reticulocyte count
Platelet count
Bleeding time
Clotting time
Prothrombin time
Peripheral Smear

Urine

Albumin
Sugar
Deposits
Bile Salts
Bile Pigments
Urobilinogen

Serum

Creatinine
Electrolytes
Bilirubin
SGOT
SGPT
SAP
Albumin
Globulin

Ascitic fluid Analysis

Total Protein

Cellular Analysis

Bone Marrow studies

Viral Markers

HBS Ag, Anti HCV Antibodies

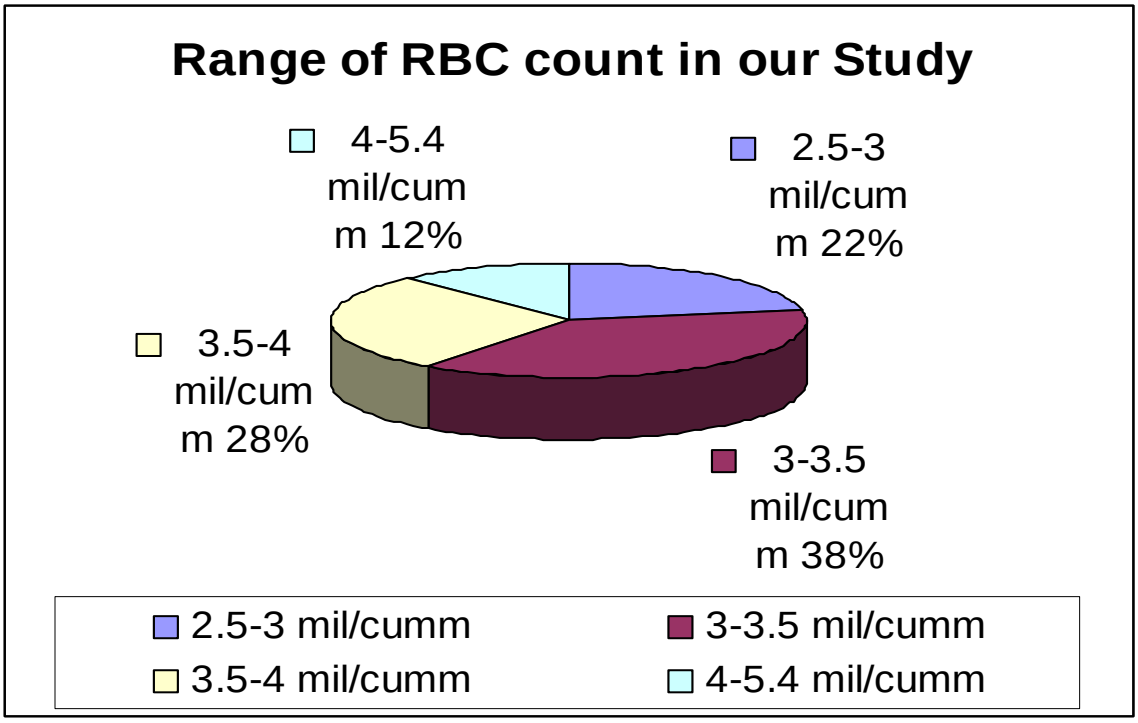
X-ray Chest

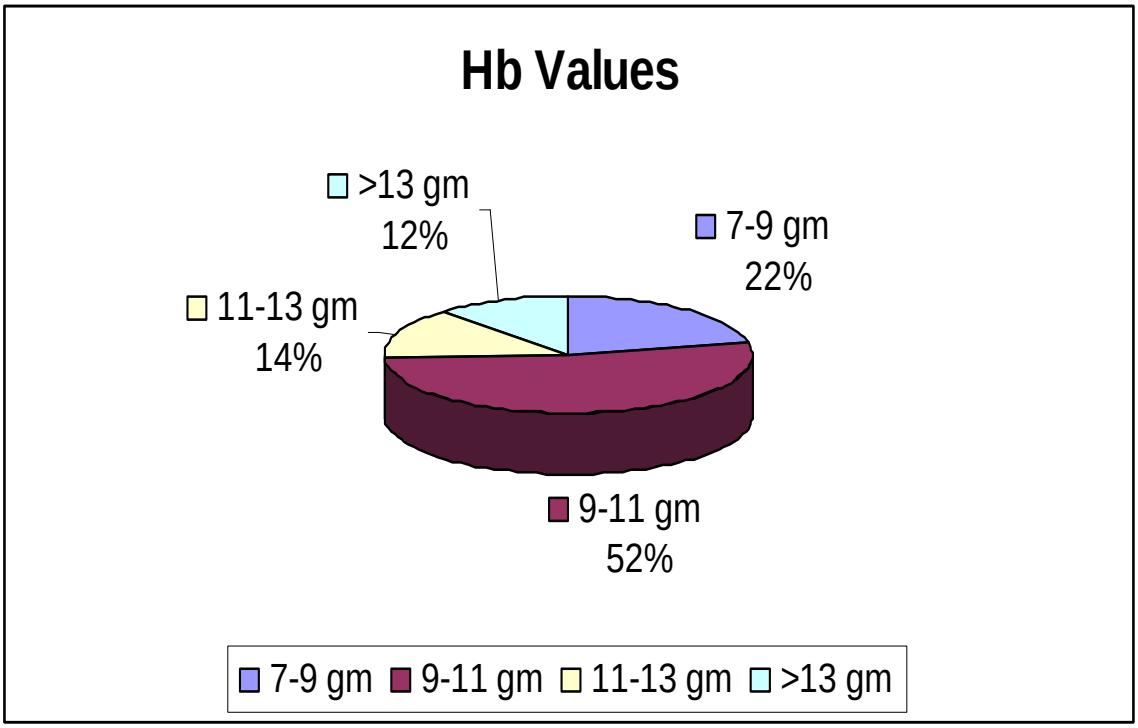
ECG

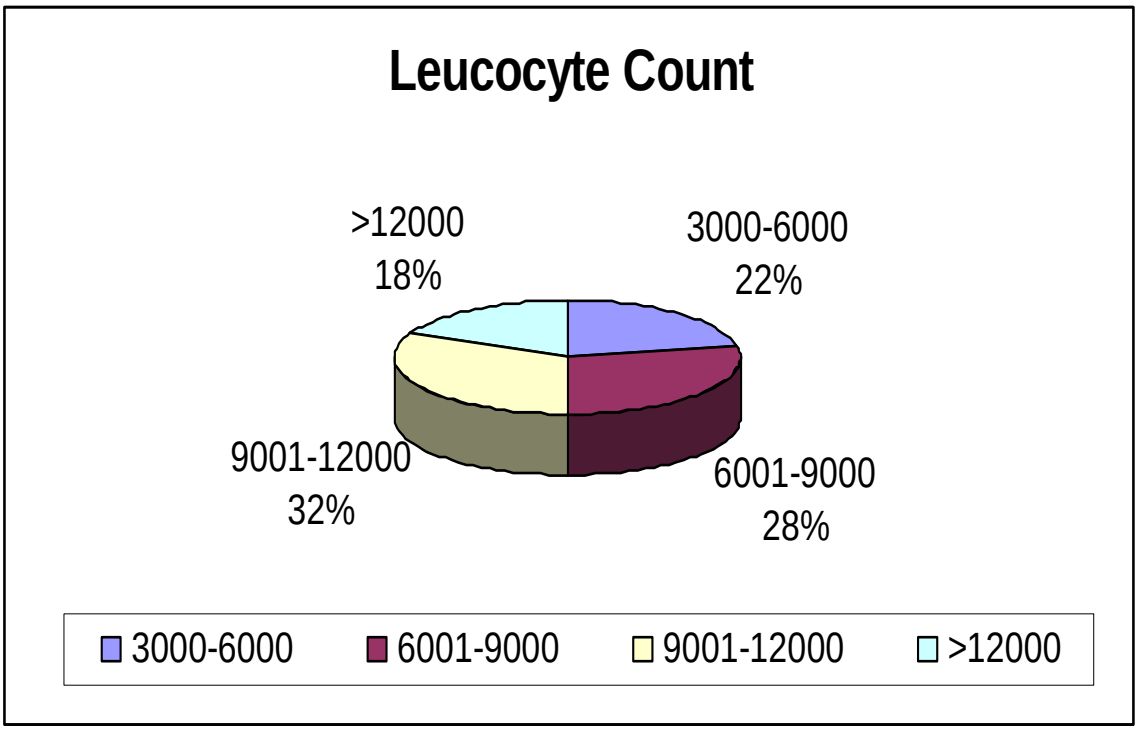
Ultra sound abdomen

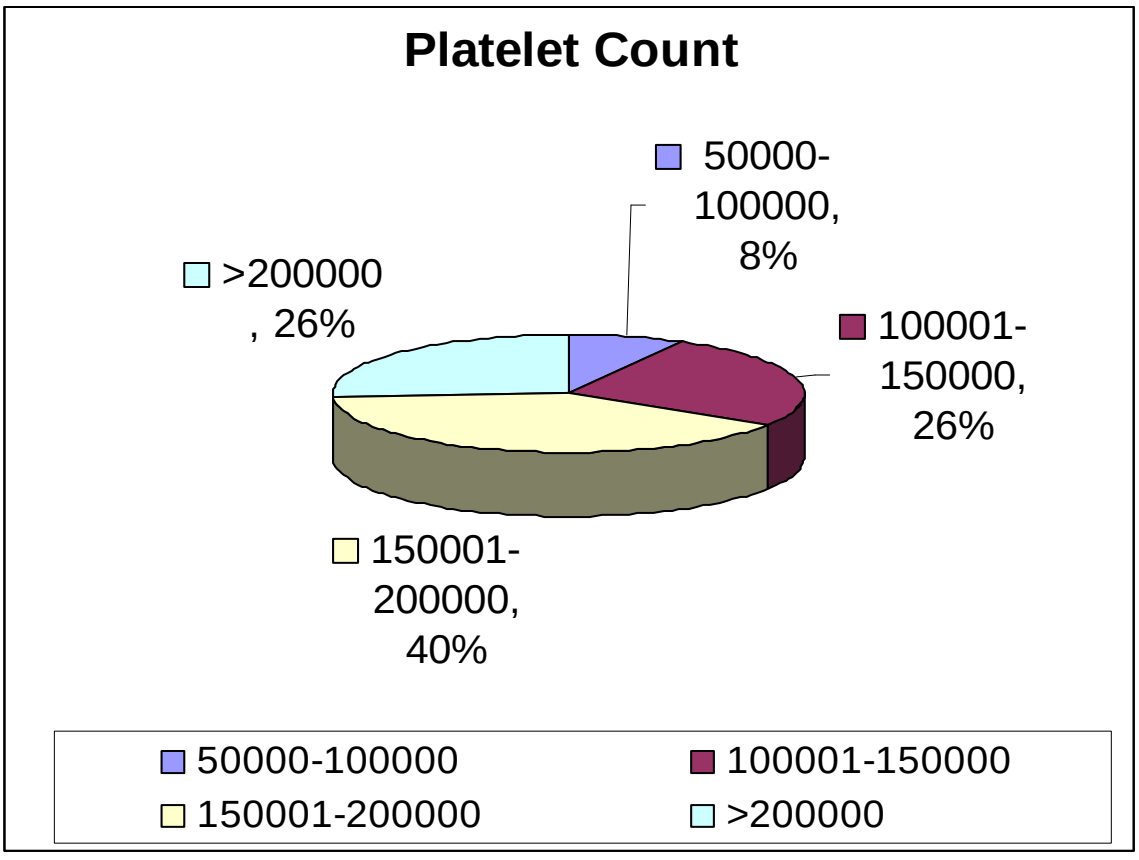
UGI Endoscopy

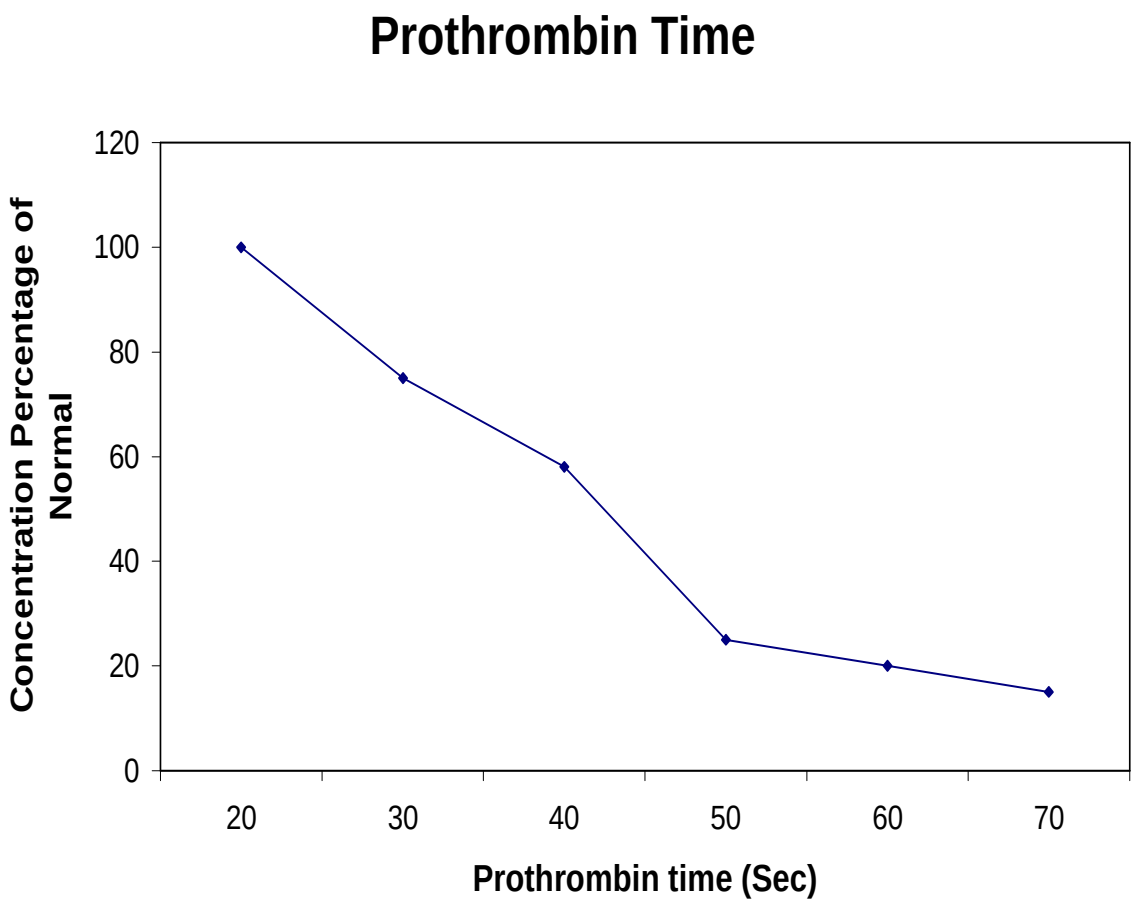
Liver Biopsy


Range of RBC count in our Study
4-5.4 mil/cumm 12%
2.5-3 mil/cumm 22%
3.5-4 mil/cumm 28%
3-3.5 mil/cumm 38%
2.5-3 mil/cumm
3-3.5 mil/cumm
3.5-4 mil/cumm
4-5.4 mil/cumm


Hb Values
>13 gm 12%
7-9 gm 22%
11-13 gm 14%
9-11 gm 52%
7-9 gm
9-11 gm
11-13 gm
>13 gm


Leucocyte Count
>12000
18%
3000-6000
22%
9001-12000
32%
6001-9000
28%
3000-6000
6001-9000
9001-12000
>12000


Platelet Count
50000-100000, 8%
>200000, 26%
100001-150000, 26%
150001-200000, 40%
50000-100000
100001-150000
150001-200000
>200000



Relationship of Prothrombin Concentration in the blood to the Prothrombin Time

DATA ANALYSIS

Our cases were analysed for the presence or absence of anaemia and the characteristic of the anaemia when present. 41 Patients (82%) had anaemia. Microcytic anaemia was demonstrable in 6 patients, normocytic anaemia was demonstrable in 25 patients and macrocytic anaemia was demonstrable in 10 patients, one patient showed dimorphic anaemia. Macrocytosis without anaemia was present in 3 cases/ Microcytic anaemia patients peripheral smear showed anisocytosis and poikilocytosis. Target cells and acanthocytes were seen in a single case. The patient with macrocytic anaemia had mean corpuscular volume more than 94 fl. There was no correlation between the severity of anaemia and the type of cirrhosis.

Table-1

Total RBC count	Cases	Percentage
2.5 – 3 Million/mm^3	11	22
3.0 – 3.5 Million/mm^3	19	38
3.5 – 4.0 Million/mm^3	14	28
4.0 – 5.4 Million/mm^3	6	12

Table – II

Hemoglobin Values

Hemoglobin %	Cases	Percentage
7 – 9	11	22
9 – 11	26	52
11 – 13	7	14
> 13	6	12

Table III

Type of RBC	Alcoholic Cirrhosis	Other Cases
Normocytic	10	19
Microcytic	6	5
Macrocytic	10	-

Table IV

Type of RBC	Anaemia	Normal HB%
Normocytic	25	6
Microcytic	6	-
Macrocytic	10	3
Total	41	9

LEUCOCYTES

The total WBC count in 4 patients is less than 4000 cells / cumm and normal counts (4000 – 11000 cells / cumm) were present in 32 patients. Leucocytosis was observed in 14 patients. There was no relationship between the total Leucocyte counts and the presence of splenomegaly or bleeding time. Since leucopenia and Leucocytosis occurred with greater frequency among patients with infection like spontaneous bacterial peritonitis and urinary tract infection. Lymphocytosis was observed in 4 patients where as lymphopenia was observed in 9 patients. Neutrophilia was observed in 8 patients.

Table V

Total count (Cells/cumm)	Number of patients	Percentage
3000 - 6000	11	22
6001 - 9000	14	28
9001 - 12000	16	32
> 12000	9	18

PLATELET

Thrombocytopenia is the term used when the platelet count is less than 1,50,000 cells/cumm. In our study thrombocytopenia was observed in 17 patients. We encountered the following values given in the table.

Table VI

Platelet Count (Cells/cumm)	Number of patients	Percentage
50000 – 1,00,000	4	8
1,00.000 – 1,50,000	13	26
1,50,000 – 2,00,000	20	40
> 2,00,000	13	26

The prothrombin time was normal in 16 patients and it is prolonged in 34 patients, bleeding time was prolonged in 4 patients who showed very low platelet count. Liver biopsy was not done for those patients because of bleeding risk. Clotting time was normal in most of the patients. Bone marrow was normocellular in 32 patients and in 14 cases it was hyperplasic. There was no hypoplastic change. There were no megaloblastic changes.

DISCUSSION

This study was conducted mainly to assess the haematological profile in cirrhotic patients. Cirrhosis of liver in various parts of the world presents some what differing clinical picture. Davidson, Sherlock, Turner contrast the behaviour of Cirrhosis in Europe and America where alcoholism is the common factor in the aetiology. Age incidence reported is usually above 35 years. Males preponderate. History of previous hepatitis is rare while ascites and jaundice is the common mode of presentation. Parotid enlargement, gynaecomastia, anaemia are common. The liver is often large. Spleen is palpable in 25% of cases. Ascites is extremely common. Serum albumin is low. In contrast non-alcoholic Cirrhosis which is relatively more common in England is reported to show female predominance. There is no particular age incidence. History of previous hepatitis is present in 30% of cases. Portal Hypertension is common. Gynaecomastia is rare, while liver is small, spleen is palpable as a rule. Coexistent peptic ulcer has been reported. Serum albumin is low in decompensated liver.

In Our series of study, most of the cases were between 20 – 65 years. Sex incidence was male and female 5:1 ratio, in our series. In our study 2 / 3 of patients belonged to urban and semi-urban areas, commonest group affected belonged to lower socio economic group. Their average monthly income was Rs.700 – 1500/-. Definite history of alcoholism for prolonged period was observed in 75% of the patients in our study.

Anaemia is a very common problem in patients with Cirrhosis of liver. The morbidity and mortality of the patients suffering from Cirrhosis of liver is much influenced by presence of associated anaemia. Correction of some reversible factors like anaemia may improve the quality of life and prolong their life span. Anaemia incidence reported by various authors ranges from 42 – 92% (Jarrold and Wilters) [21]

Different types of anaemia have been observed by various authors

	No. of cases	Incidence of Anaemia %	Type of Anaemia		
			Normo cytic %	Macro cytic %	Micro cytic %
Rosen Beng (1936)	62	42	6.4	89.7	3.9
Bianoco Jolliffec (1936)	30		26.4	52.8	19.8
Wintrobe (1936)	48	84	30.0	40.9	7.12
Malhotra (1951)	32	90.6	84.35	6.25	0.0
Sen Gupta (1958)	45	76	40	31.0	5.0
Bhatia (1961)	77	83	59.7	18.6	5.0
Mishra et al (1982)	674	91.6	79.8	5.64	5.8
Present Series	50	82	50	20	12

In our study the incident of anaemia was 82%. Wintrobe and Schumaker concluded that macrocytic anaemia resulted from defective storage and metabolism of haemopoietic principles as a consequence of inability of the damaged liver to perform normal function. (Western authors who have shown macrocytic anaemia 89.7%), normocytic anaemia (6.4%) microcytic anaemia 3.9%, with an incidence of 92% anaemia. The North Indian authors study showed Normocytic anaemia 79.8%, macrocytic anaemia 5.6%, and microcytic anaemia 5.8% with an incidence of 91.6% anaemia. In our study, Normocytic anaemia 50%, microcytic anaemia 12%, macrocytic anaemia 20% with an incidence of 82% of anaemia. Saragea and wallier came to the conclusion that GI Bleeding was the major cause of anaemia in cirrhotic.

Capps, Weinstein and Elinger showed that majority of cases of anaemia are due to hypersplenism and haemolysis. Khondaky and Rosseclin Ghata observed that Folic Acid and B12 deficiencies are cause for anaemia. Deller et al showed that the mean haemoglobin value in alcoholic cirrhosis is much lower than that of post necrotic cirrhosis. About 1-2 gm differences was observed.

There was no correlation between target cells and type of cirrhosis. Neither the type of the severity of liver disease had any influence on the frequency of macrocytosis. Mean corpuscular haemoglobin concentration was subnormal. Anisocytosis and poikilocytosis did not appear to be related to either the severity or the type of anaemia. Bone marrow in cirrhosis with Anaemia (Misra et al) showed that 52 cases were normoblastic in reaction 6 cases macronormoblastic 2 cases megaloblastic. Kimber et al in his studies of 93 cases, reported that Bone marrow was hyperplastic in 70 cases, Hypoplastic in 3 cases and normal in 20 cases.

The bone marrow was normal in 35 cases, hypoplastic in 5 cases, and hyperplastic in 6 cases. The marrow reaction was much influenced by malnutrition and blood loss. No correlation was found between marrow cellularity and anaemia either to the type of liver disease or to its severity. The major cause of anaemia was malnutrition acute and chronic blood loss, associated malarial infection, peptic ulcer and worm infestation. The existing symptoms were worsened by presence of anaemia. The morbidity was found to be directly proportional to severity of anaemia. The severity and type of anaemia was not related to type of cirrhosis.

Thrombocytopenia was also observed in our study, 34% of the patients platelet count was less than 1,50,000. Clinically except for two patients who had purpuric spots who had platelet count below 1,00,000 none of the other patients had any referable clinical signs related to thrombocytopenia. The possible mechanism of platelet deficiency in these patients probably could be due to liver cell failure and vitamin K deficiency.

Whether these patients needed any life long vitamin K supplement was a debatable one because of the paucity of clinical signs related to thrombocytopenia. Still these patients have to be carefully followed up for periodical platelets count, to prevent any bleeding complication. There was no relationship between the total WBC count and the presence of splenomegaly or bleeding time. Since leucopenia and leucocytosis and normal counts were present. However, leucocytosis occurred with greater frequency among patients with infection like spontaneous bacterial peritonitis and UTI. Lymphocytosis was observed in four patients where as lymphopenia was observed in nine patients. Neutrophilia was observed in eight patients.

SUMMARY AND CONCLUSION

This limited study aimed at the evaluation of haematological profile in liver cirrhosis patients. As expected most of the patients have some form of disturbance in the haematological profile. Majority of the patients suffered from anaemia in one form or other.

Next in the order is referable to platelet abnormalities. Thirdly small proportion of patients found to be suffering from leucocytes disturbances.

Since anaemia is found to be the major haematological abnormality in our study we aimed at correcting this problem first by giving either packed cell volume or whole blood transfusion as the case may be. This definitely as reduce the immediate mortality.

Hence, we suggest that all cirrhotic patients should be carefully monitored regarding the haematological profile and correcting these abnormalities would certainly prevent death due to anaemia, inter current infections, sepsis and hypovolemic shock due to haemorrhage.

MASTER CHART

Sl.No	Name	RBC count	Hb gm/dl.	PCV	MCV	MCHC	Type of anaemia	Total WBC count per cu.mm	differential count				Comments	Platelet count	prothrombin time in sec	Bone marrow study
									P	L	E	M				
1	Nagaraj	3.42	10	32	93.5	31.2	normocytic normochromic	9800	55	43	2	0	normal	160000	25	normal
2	Seenu	3.3	9.2	24	71	38	microcytic, normochromic	9900	69	23	8	0	normal	190000	27	hyperblastic
3	Viji	3.6	8.2	24	80.5	35.1	normocytic normochromic	8600	84	10	6	0	lymphopenia	130300	22	normal
4	Mani	4.2	13.8	40	90.5	30.4	normocytic normochromic	8200	58	36	6	0	normal	220000	20	normal
5	chandrasekar	2.9	9.2	27	93	34	normocytic normochromic	5900	72	24	4	0	normal	440000	24	hyperblastic
6	Velu	3.2	10	33	103.1	30.3	macrocytic, normochromic	10400	82	12	6	0	lymphopenia	155000	25	normal
7	Adam	3.4	10.8	30	88.2	36	normocytic normochromic	9600	78	15	7	0	lymphopenia	63000	38	normal
8	Pandian	3.64	10.5	35	96.9	30	macrocytic, normochromic	3800	78	13	9	0	leucopenia	120000	28	normal
9	Ramesh	3.42	10.1	30	96.9	33.3	normocytic normochromic	13200	74	14	11	0	leucocytosis	170000	24	normal
10	Chinnappa	4.1	13.2	39	90.5	33.8	normocytic normochromic	9900	66	32	2	0	normal	220000	22	normal

MASTER CHART

Sl.No	Name	RBC count	Hb gm/dl.	PCV	MCV	MCHC	Type of anaemia	Total WBC count per cu.mm	differential count				Comments	Platelet count	prothrombin time in sec	Bone marrow study
									P	L	E	M				
11	Gopinath	2.6	7	19	73	36.8	microcytic, normochromic	13400	80	18	2	0	leucocytosis	140000	28	hyperblastic
12	Baskar	3.8	12	34	89.4	32.2	normocytic normochromic	8900	70	25	5	0	normal	160000	22	normal
13	Bhoominath	3.4	10.4	28	82	37	normocytic normochromic	12200	73	13	14	0	leucocytosis	130000	30	normal
14	Ramnath	3.81	12.8	39	102.6	32.3	macrocytic, normochromic	9100	72	23	5	0	normal	180000	24	normal
15	Pandian	3.88	13	39	101.50	33.3	macrocytic, normochromic	3900	54	42	4	0	leucopenia	120000	32	hypoblastic
16	Palraj	2.88	9.5	28	97.2	33.9	macrocytic, normochromic	11200	74	24	2	0	leucocytosis	190000	29	normal
17	Veeraiya	3.4	8.8	25	73.5	35.4	microcytic, normochromic	4700	62	36	2	0	normal	160000	30	-
18	Seenu	3.9	13.20	40	102	33	macrocytic, normochromic	7600	58	37	5	0	normal	250000	22	hypoblastic
19	Thangavel	2.9	9	26	89.6	35.6	normocytic normochromic	13200	70	26	4	0	leucocytosis	80000	40	-
20	Yuvaraj	3.8	8	27	71	29.6	microcytic, normochromic	5500	68	30	2	0	normal	160000	27	normal

MASTER CHART

Sl.No	Name	RBC count	Hb gm/dl.	PCV	MCV	MCHC	Type of anaemia	Total WBC count per cu.mm	differential count				Comments	Platelet count	prothrombin time in sec	Bone marrow study
									P	L	E	M				
21	Raghavan	3.14	9.5	27	85.9	35	normocytic normochromic	8200	60	37	3	0	normal	210000	29	normal
22	Arjunan	3.07	9.3	28	86.2	33.2	dimorphic	10400	80	14	6	0	lymphopenia	220000	23	normal
23	Abdul	2.9	8.8	25	86.2	35.2	normocytic normochromic	7500	38	54	8	0	lymphopenia	140000	26	-
24	Kuppan	3.65	12	35	95.8	34.2	macrocytic, normochromic	5100	66	26	8	0	normal	120000	29	normal
25	Pichaiya	3.52	11	33	93	33.3	normocytic normochromic	12800	70	24	6	0	leucocytosis	190000	26	normal
26	Chinnaiyan	4.1	13.5	39	95	34.6	macrocytic, normochromic	10800	63	32	5	0	normal	202000	19	normal
27	Govindhan	3.15	10.2	29	92	35.1	normocytic normochromic	13400	80	17	3	0	leucocytosis	200000	20	-
28	Kannan	3.6	10.8	32	88.8	33.75	normocytic normochromic	8600	70	24	6	0	normal	150000	26	normal
29	Subbaiyah	2.56	8.2	23	89.8	35.6	normocytic normochromic	9800	68	24	8	0	normal	160000	27	normal
30	Saleema	3.2	9.2	30	88.2	36.6	normocytic normochromic	12900	74	22	4	0	leucocytosis	180000	27	normal

MASTER CHART

Sl.No	Name	RBC count	Hb gm/dl.	PCV	MCV	MCHC	Type of anaemia	Total WBC count per cu.mm	differential count				Comments	Platelet count	prothrombin time in sec	Bone marrow study
									P	L	E	M				
31	Pattu	2.9	7.5	21	72.4	35.1	microcytic, normochromic	3900	59	38	2	1	leucocytosis	110000	30	hyperblastic
32	Venkat	3.6	12	33	91.6	36	normocytic normochromic	7100	66	28	6	0	normal	210000	19	normal
33	Vijaya	3.24	9.6	29	80.2	33.1	normocytic normochromic	4600	49	47	4	0	lymphocytosis	150000	23	normal
34	Padma	3.08	9.4	28	90.9	33.5	normocytic normochromic	11200	64	34	2	0	normal	140000	30	normal
35	Veeran	2.56	8.2	23	89.8	35.6	normocytic normochromic	9800	68	24	8	0	normal	160000	27	normal
36	Thirumalai	3.88	13	39	100.5	33.3	macrocytic, normochromic	3900	54	42	4	0	leucopenia	120000	32	hypoblastic
37	Velan	3.07	9.3	28	86.2	33.2	dimorphic	10400	80	14	6	0	lymphopenia	220000	23	normal
38	Kadhir	2.9	8.8	25	86.2	35.2	normocytic normochromic	7500	38	54	8	0	lymphopenia	140000	26	-
39	Kumar	3.81	12.8	39	102.6	32.3	macrocytic, normochromic	9100	72	23	5	0	normal	180000	24	normal
40	Ananth	3.2	10	33	103.6	30.3	macrocytic, normochromic	10400	82	12	6	0	lymphopenia	155000	25	normal

MASTER CHART

Sl.No	Name	RBC count	Hb gm/dl.	PCV	MCV	MCHC	Type of anaemia	Total WBC count per cu.mm	differential count				Comments	Platelet count	prothrombin time in sec	Bone marrow study
									P	L	E	M				
41	Senthil	3.64	10.5	35	96.9	30	macrocytic, normochromic	3800	78	13	9	0	leucopenia	120000	28	normal
42	Umir	3.42	10	32	93.5	31.2	normocytic normochromic	9800	55	43	2	0	normal	160000	25	normal
43	Selvi	3.2	9.2	30	88.2	30.6	normocytic normochromic	12900	24	22	4	0	leucocytosis	180000	27	normal
44	Balu	3.4	8.8	25	73.5	35.2	microcytic, normochromic	4700	62	36	2	0	normal	160000	30	-
45	Palanichamy	4.1	13.5	39	95	30.4	macrocytic, normochromic	10800	63	32	5	0	normal	202000	19	hypoblastic
46	Sellaia	3.65	12	35	95.8	34.2	macrocytic, normochromic	5100	66	26	8	0	normal	120000	28	hypoblastic
47	Murugan	3.6	12	33	91.6	36	normocytic normochromic	12100	66	28	6	0	normal	210000	19	normal
48	Arul	3.3	9.2	24	71	32	microcytic, normochromic	9900	69	23	8	0	normal	109000	27	hyperblastic
49	Kapali	2.9	9.2	27	93	34	normocytic normochromic	5900	72	24	4	0	normal	440000	24	hyperblastic
50	Kesavan	4.1	13.5	39	95	34.6	macrocytic, normochromic	10800	63	32	5	0	normal	202000	19	-

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